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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/725,178	11/29/2000	Bettina Mockel	P 273989 990168 BT	8596

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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/725,178

Applicant(s)

MOCKEL ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-7,21-23,25 and 26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 5 and 7 is/are allowed.
- 6) ☒ Claim(s) 1,2,4,6,21-23,25 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/11/2003 has been entered.

Applicants amendment of the specification, claims 1, 2, 5-7, 25 and 26 and the cancellation of claims 3 and 24, Paper No. 17, 1/22/2003, and applicants amendment of claims 1, 5 and 7, Paper No. 20, 3/11/2003, is acknowledged. Claims 1, 2, 4-7 and 21-26 are at issue and are present for examination.

Applicants' arguments filed on 1/22/2003, Paper No. 17, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office actions as applied to previous claims 1-4, 6, and 21-24 and is repeated below with emphasis on now remaining rejected claim 2.

The instant claim is drawn to polynucleotides encoding a polypeptide that has at least 90% identity to SEQ ID NO: 2, wherein said polynucleotide is isolated from a coryneform bacterium.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common

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characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a single polynucleotide encoding SEQ ID NO: 2 is fully described in the form of SEQ ID NO:1, wherein SEQ ID NO: 2 has phosphoglycerate mutase activity. This description also adequately describes a genus, within the sequence identity limitations of the instant claims, of polynucleotides encoding proteins having this particular function. Those sequences that are "naturally occurring" or isolated from coryneform bacteria are a subset of this genus. The specification does not adequately describe this subset according to its structure so that one of skill in the art would be able to predict naturally occurring sequences, particularly in view of the larger genus that includes both naturally and "manufactured" sequences. Therefore, the instant claims are not adequately described.

Claims 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim is drawn to polynucleotides comprising at least 30 consecutive nucleotides of SEQ ID NO: 1, wherein said polynucleotide is a probe in a hybridization reaction to detect or to isolate a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2.

The specification, however, only provides a single representative species of SEQ ID NO: 1 encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of the claimed genus of polynucleotides by any identifying structural characteristics or properties other than the claimed polynucleotide is a "primer in a polymerase chain reaction to produce a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2" or a "probe in a hybridization reaction to detect or to isolate a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2", for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 2, 4 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide which has the amino acid sequence of SEQ ID NO: 2, wherein said polypeptide has phosphoglycerate mutase enzymatic activity, does not reasonably provide enablement for any polynucleotide encoding a polypeptide which is a mere 90%

identical to SEQ ID NO: 2, wherein said polypeptide has phosphoglycerate mutase enzymatic activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office actions Paper No. 13, 5/6/2002, and Paper No. 16, 10/20/2002, and traversed by applicants in Paper No. 15, 8/6/2002, and Paper No. 17, 9/22/2003. Upon further consideration the scope of what is considered to be enabled has changed and is explained below.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 2, 4 and 21-23 are so broad as to encompass any polynucleotide encoding a polypeptide which is at least 90% identical to SEQ ID NO: 2, wherein said polypeptide has phosphoglycerate mutase activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims, including all polynucleotides variants, both naturally occurring and engineered, of SEQ ID NO: 1 encoding a polypeptide which has a mere 90% identity to SEQ ID NO: 2. The

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claims rejected under this section of U.S.C. 112, first paragraph, place insufficient structural limits and are supported by insufficient guidance as to how to make those polynucleotides encompassed by the claimed genus. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polynucleotide having the sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass the claimed modifications and fragments of SEQ ID NO: 1, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting phosphoglycerate mutase enzymatic activity; (B) the general

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tolerance of phosphoglycerate mutase enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a phosphoglycerate mutase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the phosphoglycerate mutase enzymatic activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus encoding a polypeptide having phosphoglycerate mutase activity..

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all polynucleotides encoding a polypeptide which is at least 90% identical to SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those

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skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Sigma Catalog, 1997, pages 1019.

The Sigma catalog teaches a number of molecules di- tri- and polynucleotide molecules which are encompassed by fragments of SEQ ID NO: 1 (see for example page 1019). Claim 6 is currently drawn to an isolated polynucleotide consisting of the nucleotide sequence shown in SEQ ID NO: 1, or a fragment thereof, wherein said nucleotide sequence encodes for a polypeptide having phosphoglycerate mutase activity. As the phosphoglycerate mutase activity limitation is only stipulated for the polypeptide encoded by "the nucleotide sequence", and not the "fragment thereof", claim 6 is anticipated by the Sigma Catalog.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read "Richard Hutson", written over a horizontal line.

Richard Hutson, Ph.D.
Primary Patent Examiner
Art Unit 1652
April 18, 2003